CLAIMS

We claim:

1. A method of altering a first gene expression pattern in an isolated multipotent adult progenitor cell (MAPC) comprising:

a) introducing into a MAPC an exogenous polynucleotide molecule, wherein the exogenous polynucleotide molecule comprises i) a targeting polynucleotide sequence homologous to a genomic DNA sequence of the MAPC and ii) a donor nucleotide sequence of interest; and

b) culturing the MAPC under conditions sufficient to homologously recombine the exogenous polynucleotide molecule, such that a resultant MAPC has a second expression pattern different than the first gene expression pattern.

2. The method of claim 1, wherein the MAPC is isolated from a mouse, a rat or a human.

3. The method of claim 1, wherein the introducing is via nucleoporation.

4. The method of claim 1, further comprising differentiating the resultant MAPC.

5. The method of claim 1, wherein the exogenous DNA molecule further comprises a DNA sequence encoding a selectable marker.

6. A method of making recombinant multipotent adult progenitor cells (MAPCs) comprising:

a) culturing isolated MAPCs at low density;

b) nucleoporating the MAPC in the presence of an exogenous polynucleotide molecule, wherein the polynucleotide molecule comprises i) a targeting polynucleotide sequence homologous to a genomic DNA

sequence of the MAPC and ii) optionally a DNA sequence encoding a gene product; and

c) culturing the MAPC obtained in b) under conditions sufficient to homologously recombine the exogenous DNA molecule, thereby making a recombinant MAPC.

7. The method of claim 6, wherein the MAPCs are cultured at about 500 cells/cm^2.

8. The method of claim 6, wherein the MAPCs are isolated from a mouse, a rat or a human.

9. A recombinant MAPC produced by the method of claim 6.

10. A method of correcting a genetic defect in a mammal, wherein the defect is one or more defective nucleotide sequence(s) in the genome of the mammal that give(s) rise to defective gene expression, the method comprising:

a) culturing a MAPC from the mammal having the genetic defect;

b) introducing into the MAPC an exogenous DNA molecule, wherein the DNA molecule comprises i) a targeting DNA sequence homologous to a genomic DNA sequence of the MAPC and ii) one or more donor nucleotide sequence(s) necessary for correcting said genetic defect in said mammal,

c) culturing the MAPC under conditions sufficient to homologously recombine the exogenous DNA molecule into the genome of the MAPC, thereby obtaining a genetically altered MAPC;

d) selecting said genetically altered MAPC; and

e) transplanting said genetically altered MAPC into the mammal;

wherein the selecting and transplanting can be done in any order or simultaneously.

11. The method of claim 10, wherein the mammal is a mouse, a rat or a human.

12. The method of claim 10, wherein the genetic defect is in the gene encoding FANCC.

13. The method of claim 10, wherein the introducing is via nucleoporation.

14. The method of claim 12, wherein the selecting is by treatment of the MAPCs with a dose of mitomycin C, wherein the dose is toxic to MAPCs not expressing the gene product and non-toxic to said genetically altered MAPC expressing the gene product.

15. The method of claim 10, further comprising differentiating the genetically altered MAPC prior to or upon transplanting.

16. The method of claim 10, wherein the exogenous DNA molecule further comprises a DNA sequence encoding a selectable marker.

17. The method of claim 16, wherein the DNA sequence encoding the selectable marker is flanked at each of the 5' and 3' ends by a *lox* P site.

18. A genetically altered MAPC comprising an exogenous polynucleotide molecule homologously recombined into the genome of a MAPC.

19. A differentiated cell arising from the genetically altered MAPC of claim 18.

20. A method of expressing a functional gene product of interest in an isolated MAPC having a defective nucleotide sequence from which a functional gene product cannot be expressed, the method comprising:

a) introducing into the MAPC an exogenous DNA molecule, wherein the DNA molecule comprises i) a targeting DNA sequence

homologous to a genomic DNA sequence of the MAPC and ii) a donor nucleotide sequence corresponding to the defective nucleotide sequence; and

b) culturing the MAPC under conditions sufficient to homologously recombine the exogenous DNA molecule into the genome of the MAPC, thereby expressing the functional gene product of interest in said MAPC.